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Cell-free DNA (cfDNA) workflow for the risk definition of dose-limiting and recurrent neutropenia in patients treated with first-line endocrine therapy (ET) and cyclin-dependent kinase 4/6 inhibitors (CDK4/6i) for metastatic breast cancer (MBC)

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Background

- We previously observed the differential dinamics of cfDNA during treatment with CDK4/6i in hormone receptor (HR)-positive/HER2- negative MBC (luminal MBC).
- We now hypothesize a potential association between leucocytes and medium/long cfDNA fractions (mainly deriving from citolysis).
- Aim of the study was to evaluate the feasibility of a cfDNA-based workflow as a novel tool for assessing the risk of treatment-induced recurrent-neutropenia (rec-NP) and NP-induced CDK4/6i dose reduction (DR) in patients (pts) treated for luminal MBC.

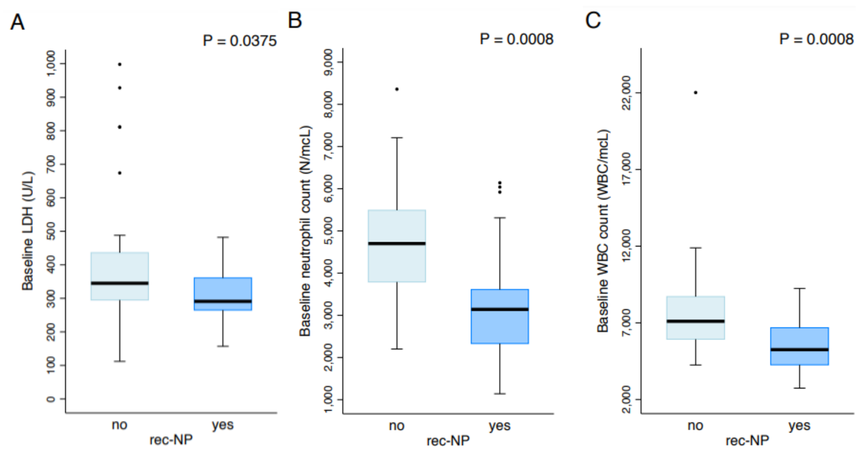
Methods

- 83 luminal MBC patients (pts) treated with first line ET and CDK4/6i
- cfDNA was characterized through droplet digital PCR (ddPCR) based on different ACTB DNA fragments lengths: short (s), medium (sl) and long (l).
- Blood samples were collected at baseline (BL) and after 3 months (E1).
- Associations between clinical characteristics, cfDNA, rec-NP (≥3 NP events) and DR were explored through Kruskal Wallis

Conclusions

- **cfDNA could have additional applications apart from tumor-biology in metastatic breast cacancer.**
- **cf-DNA can be explored as a risk-defining factor for drug-related adverse events, such as CDK4/6i-induced dose-limiting neutropenia.**
- **Additional investigations are planned to further refine the concept.**

Figure A-B-C. Variables tested and rec-NP.



Results

Table 1. Variables tested and DR.

Variables tested	P
De novo metastatic (lower risk)	0.0304
High ACTB_sl BL	0.0096

Table 2. Pts and NG3-G4.

N°pts	83
NG3-G4	46 (55%)
Rec-NP	29 (35%)
Dose Reduction after NG3-G4	12 (26%)

Table 3. Variables tested not significant.

ACTB_sl and Rec-NP	> 0.05
Low WBC BL and DR	> 0.05
Low N BL and DR	> 0.05
Low LDH and DR	> 0.05
Liver met and DR	> 0.05
Bone met and DR	> 0.05

Conflict of interest: authors declare there is no relevant conflict of interest

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